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EXAMINER	
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ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/11/98

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☐ THE PERIOD FOR RESPONSE:

a) ☐ is extended to run _____ or continues to run _____ from the date of the final rejection

b) ☐ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition , and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☑ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☑ Applicant's response to the final rejection, filed 5/7/98 has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. ☑ The proposed amendments to the claim and /or specification will not be entered and the final rejection stands because:

   a. ☐ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.

   b. ☑ They raise new issues that would require further consideration and/or search. (See Note).

   c. ☐ They raise the issue of new matter. (See Note).

   d. ☑ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

   e. ☐ They present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: Amendment of the claims would require reinstatement of double patenting rejection from Paper #7, 102(a) drawn to Murphy et al from Paper #7, 102(a) drawn to Berd et al from Paper #7, 103 drawn to Berd et al in view Fujiwara et al & Fujiwara et al in Paper #7 + 103 rejection of claims 44 + 45 + 103 rejection of cl. 47

2. ☐ Newly proposed or amended claims _____ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.

3. ☑ Upon the filing an appeal, the proposed amendment ☐ will be entered ☑ will not be entered and the status of the claims will be as follows:

Claims allowed: None
Claims objected to: None
Claims rejected: _____

However; If the amendment to the claims were to be entered all rejection of claims in Paper #23

☑ Applicant's response has overcome the following rejection(s): UNDER 35 USC 112, 1st & 2nd paragraph would be withdrawn

4. ☑ The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection because See attached.

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficent reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☐ Other

If the amendment to the claims were to be entered

1. Claims 2, 3, 5-7, 10, 22, 24-28, 34-42 and 45-48 would be rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of US Patent No. 5,290,551 for essentially the reasons, drawn to the rejection of claim 1-6 and 20, disclosed in Paper No. 7, pages 9-10 .

2. Claims 2, 3, 5-7, 10, 22, 24-28, 34-42, 45, 46 and 48 would be rejected under 35 U.S.C. § 102(a) as being anticipated by Murphy et al (Lab. Investigation, 1990, 62(1)70A, essentially for the reasons, drawn to claims 1-6 and 22-29, disclosed in Paper No. 7, page 10.

Applicant argues that (a) Murphy et al is not available as a reference because of the Declaration of Dr. David Berd under 35 CFR 1.132 filed with the Response mailed August 4, 1997, (b) Murphy et al does not disclose nor suggest eliciting a DTH or other inflammatory response, much less prolongation of survival. The arguments have been noted but have not been found persuasive because (a) the Berd Declaration (Paper No. 21) does not overcome the rejection because there is no statement that the other authors did not take part in the conception of any of the subject matter disclosed and are accordingly not co-inventors, nor is there a statement that the work done by the other authors that relates to the present invention was done under the direction and control of Dr. Berd and therefore the Declaration is considered to be incomplete and ineffective to overcome the reference, (b) although Murphy et al does not disclose or suggest nor suggest eliciting a DTH or other inflammatory response, much less prolongation of survival

these effects would be inherent properties of the methods because the method of the prior art comprises the same method steps as claimed in the instant invention thus the claimed method is anticipated because the method will inherently lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

3. Claims 2, 3, 5-7, 10, 22, 24-28, 34-42, 45, 46 and 48 would be rejected under 35 U.S.C. § 102(b) as being anticipated by Berd et al (Proc. AACR Annu Meet 30:382, 1989), essentially for the reasons, drawn to claims 1-7 and 22-29, disclosed in Paper No. 7, pages 10-11.

Applicant argues that withdrawal of this rejection is proper based on the remarks in Paper No. 20, Pages 19-22.

In Paper No. 20, Applicant argues that (a) the 1989 abstract does not suggest that preparation involving haptenized melanoma cells would be as good as, let alone better than prior preparations thus the abstract discloses insufficient information, (b) the vaccine and treatment of the present invention causes an unexpectedly higher immunity directed at the tumor, (c) there is no teaching or suggestion of an inflammatory immune response or of eliciting activated T lymphocytes to the tumor, nor any suggestion for treating any other type of cancer. The argument has been noted but has not been found persuasive because Applicant is arguing limitations not recited in the claims as presently constituted nor does the abstract disclosure insufficient information as it clearly discloses both the method and composition of the instant claims, (b) it is not clear to what the "higher immunity" refers, is this referring to vaccines and methods without DNP or other melanoma cell-DNP conjugate based methods and compositions, (c) the method of the prior art

comprises the same method steps as claimed in the instant invention thus the claimed method is anticipated because the method will inherently lead the claimed effects.

3. Claims 2, 3, 5-7, 10, 22, 24-28, 34-42, 45, 46 and 48 would be rejected under 35 U.S.C. § 103 as being unpatentable over Berd et al (Cancer Res. 1986, 46:2572-2577) in view of Fujiwara et al (J. Immunol. 1980, 124:863), Fujiwara (J. Immunol. 1984, 133:510-514) and Geczy et al (J. Immunol., 1970, 19:189-203 essentially for the reasons, drawn to claims 1-7, 10 and 22-29, disclosed in Paper No. 7, pages 13-14.

Applicant argues that withdrawal of this rejection is proper based on the remarks in Paper No. 20, Pages 22-24.

In Paper No. 20, Applicant argues that (a) the Berd references fails to teach or suggest an effective vaccine or methods of treatment of various tumors using hapten modified cells (b) the Geczy reference does not provide further expectation of success even if combined with the teachings of the 1989 Berd reference since the reference is only cited for its limited teaching that dinitrochlorobenzene and 1-fluoro-2,4-dinitrochlorobenzene may be interchangeable. The arguments have been noted but have not been found persuasive (a) for the reasons disclosed above (b) Applicant has argued and discussed the references without discussing either of the Fujiwara references or Berd reference applied in this rejection and thus has not addressed the combined teachings. It must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which

made up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the cited references taken in combination. In re Young, 403 F.2d 754, 159 USPQ 725 (CCPA 1968); In re Keller 642 F.2d 413,208 USPQ 871 (CCPA 1981).

3. Claims 43, 44 and 47 would be rejected under 35 U.S.C. § 103 as being unpatentable over McCune et al (Cancer, , 1981, 47:1984-1987) or McCune et al (Cancer, 1979, 43:1619-1623) in view of Berd et al (Cancer Res. 1986, 46:2572-2577) Fujiwara et al (J. Immunol. 1980, 124:863), Fugiwara (J. Immunol. 1984, 133:510-514) and Geczy et al (J. Immunol., 1970, 19:189-203 essentially for the reasons, drawn to claims 1-7, 10 and 22-29, disclosed in Paper No. 7, pages 13-14.

The claims are drawn to a method for treating a malignant tumor in a human patient comprising administering to the patient a composition comprising a therapeutically effective amount of human tumor cells that are conjugated to a hapten, are of the same tumor type as a malignant tumor of a patient for treatment of whom the composition is intended, are autologous to said patient, have been rendered incapable of growing in the body of a human upon injection, said composition eliciting at least one of the following upon administration to said patient with an adjuvant, (I) an inflammatory immune response against the tumor, (ii) a delayed-type hypersensitivity response against the tumor or (iii) activated T lymphocytes that infiltrate the tumor wherein said malignant tumor is not melanoma wherein administration is repeated at least 6 times at spaced apart intervals..

McCune et al (1981) teach a method of treating renal carcinoma comprising administering to a patient a composition of autologous irradiated renal carcinoma

cells admixed with an adjuvant (see abstract), said composition to be injected weekly up to 14 weeks (p. 1985).

McCune et al (1979) teach a method of treating renal cancer, melanoma, breast cancer, lung cancer and colon cancer comprising administering to a patient a composition of autologous irradiated tumor cells admixed with an adjuvant (see Table 2 and abstract) with multiple injections ((see Treatment Schedule, p. 1620).

McCune et al (1979 and 1981) teach as set forth above but do not teach method for treating a malignant tumor in a human patient comprising administering to the patient a composition comprising a therapeutically effective amount of human tumor cells that are conjugated to a hapten, said composition eliciting at least one of the following upon administration to said patient with an adjuvant, (I) an inflammatory immune response against the tumor, (ii) a delayed-type hypersensitivity response against the tumor or (iii) activated T lymphocytes that infiltrate the tumor.

Berd et al, Fujiwara et al (J. Immunol. 1980), Fugiwara (J. Immunol. 1984) and Geczy et al teach as set forth above.

It would have been *prima facie* obvious to one of ordinary skill in the art and one of ordinary skill in the art would have been motivated to combine the above references to produce the instantly claimed method essentially for the reasons set forth in Paper No. 7 pages 13-14. Further, although the references do not teach that the composition elicits at least one of (i) an inflammatory immune response against the tumor, (ii) a delayed-type hypersensitivity response against the tumor or (iii) activated T lymphocytes that infiltrate the tumor these effects would be inherent

properties of the composition and method of the combined references because the method of the prior art comprises the same method steps as claimed in the instant invention thus the claimed method is anticipated because the method will inherently lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

LILA FEISEE
SUPERVISORY PATENT EXAMINER